Amendments to the Specification:

Please replace the paragraph on page 6, lines 17-31, with the following amended paragraph:

Like Patched, HTPL-L contains a Patched domain (Pfam, Washington University, St. Louis, web site)~~(http://pfam.wustl.edu/hmmsearch.shtml)~~, a Sterol-sensing domain (SSD, GenomeNet website, Kyoto University Bioinformatics Center~~http://motif.genome.ad.jp/~~) and twelve transmembrane domains (SMART, European Molecular Biology Laboratory, Heidelberg, web site)~~(http://smart.embl-heidelberg.de/smart/show_motifs.pl)~~. The Patched domain in HTPL-L covers amino acid sequences 166 – 952 of HTPL-L. The SSD domain in HTPL-L covers amino acid sequences 383 – 540 of HTPL-L. The presence of these domains in HTPL-L suggest that HTPL-L, like Patched and other Patched domain containing proteins, is involved in the Hedgehog signaling pathway (see background section). Because of the presence of the premature stop codon, HTPL-S contains a partial Patched domain, a complete Sterol-sensing motif and seven transmembrane domains. The presence of these domains in HTPL-S suggests that HTPL-S is also involved in the Hedgehog signaling pathway.

Please replace the paragraph on page 6, line 32 through page 7, line 15, with the following amended paragraph:

Other signatures of the newly isolated HTPL proteins were identified by searching the PROSITE database (Expert Protein Analysis System (ExPASy) web site)~~(http://www.expasy.ch/tools/scnpsit1.html)~~, and the list below is for both HTPL-L and HTPL-S unless specified otherwise. These include seven *N*-glycosylation sites (192 – 195, 275 – 278, 279 – 282, 530 – 533, 678 – 681, 692 – 695 and 737 – 740), one cAMP- and cGMP-dependent protein kinase phosphorylation site (201 – 204), seven protein kinase C phosphorylation sites (194 – 196, 200 – 202, 508 – 510, 561 – 563, 662 – 664, 746 – 748, and 759 – 761; plus one for HTPL-L at 800 - 802), twelve Casein kinase II phosphorylation sites (19 – 22, 36 – 39, 62 – 65, 79 – 82, 190 – 193, 215 – 218, 219 – 222, 225 – 228, 230 – 233, 572 – 575, 597 – 600, and 740 - 743), two tyrosine kinase phosphorylation ~~site~~sites (329 – 335, and 681 – 688; plus one for HTPL-L at 887 - 893), four *N*-myristoylation sites (307 – 312, 418 – ~~4223~~423, 504 – 509, and 535 – 540; plus one for HTPL-L at 935 - 940), and a single amidation site at 541 -544.

Please replace the paragraph on page 20, lines 3-15, with the following amended paragraph:

For purposes herein, percent identity of two nucleic acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which

procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at the National Center for Biotechnology Information (NCBI) web site.

~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html.~~

To assess percent identity of nucleic acids, the BLASTN module of BLAST 2 SEQUENCES is used with default values of (i) reward for a match: 1; (ii) penalty for a mismatch: -2; (iii) open gap 5 and extension gap 2 penalties; (iv) gap X_dropoff 50 expect 10 word size 11 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 82, lines 24-30, with the following amended paragraph:

Bacterial cells can be rendered electrocompetent — that is, competent to take up exogenous DNA by electroporation — by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided online in Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~.

Please replace the paragraph on page 84, lines 1-19, with the following amended paragraph:

For chemical transfection, DNA can be coprecipitated with $CaPO_4$ or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for

$CaPO_4$ transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN, USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found online in Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~. *See also*, Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000) (ISBN 1-881299-34-1), incorporated herein by reference in its entirety.

Please replace the paragraph on page 86, lines 4-16, with the following amended paragraph:

For purposes herein, percent identity of two amino acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at the National Center for Biotechnology Information (NCBI) website.

~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html,~~ To assess percent identity of amino acid sequences, the BLASTP module of BLAST 2 SEQUENCES is used with default values of (i) BLOSUM62 matrix, Henikoff *et al.*, *Proc. Natl. Acad. Sci USA* 89(22):10915-9 (1992); (ii) open gap 11 and extension gap 1 penalties; and (iii) gap x_dropoff 50 expect 10 word size 3 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 139, lines 3-7, with the following amended paragraph:

Motif searches using Pfam (Washington University, St. Louis, web site)~~(http://pfam.wustl.edu)~~, SMART (European Molecular Biology Laboratory, Heidelberg, web site)~~(http://smart.embl- heidelberg.de)~~, and PROSITE pattern and profile databases (Expert Protein Analysis System (ExPASy) web site)~~(http://www.expasy.ch/prosite)~~, identified several known domains shared with Patched, including the Patched domain and the Sterol-sensing domain.

Please replace the paragraph on page 139, lines 16-30, with the following amended paragraph:

Like Patched, HTPL-L contains a Patched domain (pfam, Washington University, St. Louis, web site)~~(http://pfam.wustl.edu/hmmsearch.shtml)~~, a Sterol-sensing domain (SSD, GenomeNet website, Kyoto University Bioinformatics Center)~~(SSD,~~

~~http://motif.genome.ad.jp/)~~ and twelve transmembrane domains (SMART, European Molecular Biology Laboratory, Heidelberg, web site)~~(http://smart.embl-heidelberg.de/smart/show_motifs.pl)~~. The Patched domain in HTPL-L covers amino acid sequences 166 – 952 of HTPL-L. The SSD domain in HTPL-L covers amino acid sequences 383 – 540 of HTPL-L. The presence of these domains in HTPL-L suggest that HTPL-L, like Patched and other Patched domain containing proteins, is involved in the Hedgehog signaling pathway (see background section). Because of the premature stop of protein translation, HTPL-S contains a partial Patched domain, a complete Sterol-sensing motif and seven transmembrane domains. The presence of these domains in HTPL-S suggests that HTPL-S is also involved in the Hedgehog signaling pathway.

Please replace the paragraph on page 139, line 31 through page 140, line 15, with the following amended paragraph:

Other signatures of the newly isolated HTPL proteins were identified by searching the PROSITE database (Expert Protein Analysis System (ExPASy) web site)~~(http://www.expasy.ch/tools/scnpsit1.html)~~, and the list below is for both HTPL-L and HTPL-S unless specified otherwise. These include seven *N*-glycosylation sites (192 – 195, 275 – 278, 279 – 282, 530 – 533, 678 – 681, 692 – 695 and 737 – 740), one cAMP- and cGMP-dependent protein kinase phosphorylation site (201 – 204), seven protein kinase C phosphorylation sites (194 – 196, 200 – 202, 508 – 510, 561 – 563, 662 – 664, 746 – 748, and 759 – 761; plus one for HTPL-L at 800 - 802), twelve Casein kinase II

phosphorylation sites (19 – 22, 36 – 39, 62 – 65, 79 – 82, 190 – 193, 215 – 218, 219 – 222, 225 – 228, 230 – 233, 572 – 575, 597 – 600, and 740 - 743), two tyrosine kinase phosphorylation site (329 – 335, and 681 – 688; plus one for HTPL-L at 887 - 893), four *N*-myristoylation sites (307 – 312, 418 – 4223, 504 – 509, and 535 – 540; plus one for HTPL-L at 935 - 940), and a single amidation site at 541 -544.

Please replace the paragraph on page 140, lines 24-29, with the following amended paragraph:

Transcription factor binding sites were identified using a web based program (GenomeNet website, Kyoto University Bioinformatics Center)~~(http://motif.genome.ad.jp/)~~, including binding sites for homeo domain factor Nkx-2.5/Csx (625 - 631 bp), for USF (891 - 898 bp) and for CdxA (399-405 and 612 - 618 bp, with numbering according to SEQ ID NO: 23), amongst others.

Please replace the paragraph on page 145, lines 9-17, with the following amended paragraph:

Prostate cancer is the second leading cause of male cancer deaths in the United States (National Center for Biotechnology Information (NCBI) website)~~(http://www.ncbi.nlm.nih.gov/entrez/)~~. A genetic locus, designated prostate adenocarcinoma 1 (PAC1), is involved in tumor suppression of human prostate carcinoma. Sanchez *et al., Proc. Nat. Acad. Sci.* 93:2551-2556 (1996). HTPL is a

candidate gene for PAC1 as it maps to the same chromosomal region. Alternatively, mutations of HTPL could also lead to other diseases, such as those listed in Table 3.